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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,632	BURCH ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 47-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (e.g., see 7/17/07 response). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/17/07 has been entered. Claims 38 and 47-52 were pending. Applicants amended claim 38. No claims were added or canceled. Therefore, claims 38 and 47-52 are still pending and examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. All rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC 103

3. Claims 38, 47, 48, 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. US Pat. No. 4,569,937 (2/86) and Tanaka et al., Arzneimittel-Forschung (1992) Vol. 42(7) pages 935-44.

The instant claims briefly recite a method of effectively treating pain in humans

comprising orally administering to a human patient an oral dosage form comprising analgesic compounds consisting essentially of (i) N-[3-formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide and/or at least one pharmaceutically acceptable salt thereof; and (ii) oxycodone and/or at least one pharmaceutically acceptable salt thereof.

Baker et al. teach pharmaceutical compositions for relieving pain in humans comprising a combination of: a. a narcotic analgesic (preferably oxycodone: see formulations col. 4-8; patent claims), or a pharmaceutically acceptable salt thereof; and b. ibuprofen (a non-steroidal anti-inflammatory drug or NSAID: see col. 1-2), or a pharmaceutically acceptable suitable salt thereof, in a weight ratio of about 1:800 (e.g. .001:1) to 1:1 (compare to present claim 47:See col. 2) with oxycodone amounts of about 5 mgs-600mgs (compare to present claim 52).

The Baker reference teaches oral administration, which can be coadministered in a single dosage forms (e.g. see col. 3-8) or sequentially administered (e.g. col. 8-9 ; "... mice are dosed sequentially..."). The oral dosage forms include "sustained release" formulations (e.g. tablets, capsules, etc: see col. 3-4, especially col. 4). The Baker et al. reference teach that dose ratios can be adjusted and that the analgesic activity of the combined oxycodone and ibuprofen activity is "unexpectedly enhanced" or synergistic i.e. the resulting activity is greater than the activity expected from the sum of the activities of the individual components, thereby permitting reduced dosages of narcotic analgesics (e.g. oxycodone) AND which diminishes adverse side effects (e.g. addiction) and toxicity which would result from the otherwise required amounts of the individual drug components resulting from high dosages of oxycodone or NSAID's such as ibuprofen. See e.g. col. 1-2; col. 3, lines 19-32. Accordingly, Baker would teach the use of therapeutic and subtherapeutic amounts of oxycodone and/or ibuprofen in view of the additive or synergistic

nature of the combinations and the desire to reduce the toxicity and/or side-effects of both agents; and as required by the doctor for his/her particular patient, including dosage optimization e.g. dosage overlapping of active ingredients. See e.g. col. 3 where dosage is modified to suit the particular patient.

Baker et al. further teach in view of the test results of analgesic activities of oxycodone and ibuprofen, it is possible to predict the range of maximum potentiating dosages for man, and utilizing the data from the present invention and the equivalent ratios in man, it is predicted that oxycodone amounts and the ratio of the oxycodone and ibuprofen for the oral dosage in man (i.e., see columns 12-13).

The Baker analgesic composition differs from that presently claimed in that it fails to teach the substitution of T-614 (N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl) for ibuprofen into the Baker compositions.

Tanaka et al. teach that T-614 possesses superior analgesic potency, as compared to ibuprofen, against inflammatory pain and antigen-induced arthritic pain in rats with virtually no gastrointestinal ulcerogenic action and no affect on water/sodium excretion (e.g., see Tanaka et al., Summary).

Accordingly, one of ordinary skill in the art would have been motivated to substitute T-614 for ibuprofen in the Baker reference compositions in light of the Tanaka reference teaching that ibuprofen is more analgesically potent with less side effects (e.g. as compared to ibuprofen) in animal models. Additionally, it is noted that the instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two (or more) compositions each of which is taught by the

prior art to be useful for the same purpose. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Baker reference analgesic composition by substituting T-614 for ibuprofen in light of the benefits of T-614 (increased potency/decreased side effect as compared to ibuprofen) as taught by the Tanaka reference.

Alternatively, it is submitted that the mere substitution of one component for another to yield predictable results represents a *prima facie* case of obviousness whether a "teaching, suggestion, or motivation" exists or not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *12 (2007). Here, it would be obvious to make a simple substitution of T-614 for ibuprofen because it was known at the time of filing that the both provided the same antiinflammatory/analgesic relief (e.g., see Tanaka et al., Summary). Thus, the substitution one drug for another would have led to the same "predictable" results, namely, the aforementioned antiinflammatory/analgesic relief.

Response

4. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that there is no motivation to combined the Baker and Tanaka references (e.g., see 7/17/07 Response, page 6, middle paragraph).

[1] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Baker reference analgesic composition by substituting T-614 for ibuprofen in light of the benefits of T-614 (increased potency/decreased side effect as compared to ibuprofen) as taught by the Tanaka reference.

In addition, it is submitted that the mere substitution of one component for another to yield predictable results represents a *prima facie* case of obviousness whether a "teaching, suggestion, or motivation" exists or not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *12 (2007). Here, it would be obvious to make a simple substitution of T-614 for ibuprofen because it was known at the time of filing that the both provided the same antiinflammatory/analgesic relief (e.g., see Tanaka et al., Summary). Thus, the substitution one drug for another would have led to the same "predictable" results, namely, the aforementioned antiinflammatory/analgesic relief.

[2] Applicants argue, "It appears that the Examiner is overlooking the fact that the Baker reference utilizes ibuprofen because of its enhanced analgesic effect it has with oxycodone. There is nothing in the Tanaka reference to suggest that [T-614] would have this effect ... The Baker reference is therefore limited to combinations wherein the NSAID is ibuprofen and does

not teach or suggest that the purported 'unexpectedly enhanced analgesic activity' would occur with an NSAID which is different than ibuprofen" (e.g., see 7/17/07 Response, page 6, last paragraph).

[2] The Examiner is unaware of any *per se* rule that necessarily limits the teachings of a reference to its preferred "synergistic" embodiments or teachings to certain locations within the document itself (e.g., the experimental results). To the contrary, a reference is good for all that it teaches to one of ordinary skill in the art, *In re Fritch*, 972 F.2d 1260, 1264, 23 USPQ2d 1780, 1782 (Fed. Cir. 1992), and is not limited to the particular invention described and to be protected by the patent, *EWP Corp. v. Reliance Universal Inc.*, 755 F.2d 898, 907, 225 USPQ 20, 25, (Fed. Cir.1985), the specific examples disclosed, *In re Fracalossi*, 681 F.2d 792, 794 n.1, 215 USPQ 569, 570 n.1 (CCPA 1982); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976), or preferred embodiments. *In re Mills*, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972). Here, Baker et al. clearly teach the use of a general class of "analgesic combinations" to relieve pain and reduce side effects that would otherwise be required by administration of the analgesic alone (e.g., see Baker et al., column 1, lines 12-17, "More active analgesic combinations are in constant demand because they offer the attractive possibility of relieving pain with reduced dosages thereby diminishing the expected side effects and toxicity that would result from the otherwise required higher dosages"). The fact that Baker et al. classifies their results as "unexpected" only serves to support this conclusion. That is, Baker et al. must have been adequately motivated to combine these analgesics "before" they realized the synergistic value of the combination (otherwise the result would not have been "unexpected" as purported). This is further supported by the express language of the patent wherein Baker et al. state, "[a]

continuing goal is to be able to reduce the dosage of such narcotic analgesics by combining the m with non-addicting ingredients while still maintaining a high level of analgesia [i.e., whether the compounds exhibit a synergistic effect or not]" (e.g., see Baker et al., column 2, lines 5-8; see also more generally column 1 and 2 disclosing several examples of analgesic combinations including various NSAIDs including combinations that do not possess a synergistic effect; see especially column 1, lines 36-37, "there is no suggestion that the combination had a synergistic effect; see also lines 27-29, "Sunshine provides no evidence or suggestions of other than an additive analgesic effect for the combinations").

Furthermore, Tanaka et al. explicitly state that T-614 is better than ibuprofen in terms of its potency/decreased side effects and Baker et al. does not refute this position (i.e., it is undisputed that T-614 is a good substitute for ibuprofen). Thus, a person of ordinary skill in the art would expect favorable results from this substitution. In addition, Baker et al. is not limited to ibuprofen as purported. For example, Baker et al. state, "This patent [referring to Sunshine] discloses that the analgesic effect of the combination of a selected NSAID and a selected narcotic analgesic is greater than for either alone" (e.g., see column 1, lines 22-25). It does not state, contrary to Applicants' assertions, that the analgesic effect is only greater for ibuprofen. Whether another analgesic would be "unexpectedly" better is immaterial. The reference still provides ample motivation to combine an NSAID with a selected narcotic analgesic. That is, the fact that "some" increased benefit would be obtained is enough. For example, the facts of the instant case and the conclusion of obviousness made by the Examiner are somewhat similar to the facts and decision of the Court in, Syngenta Seeds, Inc., v. Monsanto Co., (Fed. Cir. 2007), opinion decided on May 3, 2007. In this case, the Court found that claims directed to a transgenic

corn plant that produces the Bt protein, having a foreign DNA nucleic acid coding sequence with a G+C content of at least about 60%, to be obvious in view of the Barton reference. Barton taught that Bt expression is improved through the use of codons preferred by the native plant, that Bt has a high proportion of A+T codons, but that plants generally have a bias towards codons rich in G+C. Syngenta argued that although the general teaching for substituting G+C codons may have been obvious, that the "more than 60%" limitation would not be obvious." The Court disagreed, and replied:

> "It is true, as Syngenta argues, that the quoted portion of the Barton application suggests that positive results could be achieved without modifying the entire DNA sequence. But the entire quoted statement [in Barton], including the conclusion that a complete codon substitution "might still be expected to increase efficiency of expression," plainly constitutes a suggestion that some increased efficiency of expression could be achieved by producing a synthetic

Here, as in Syngenta, at least some "increased efficiency" would be obtained by combining an NSAID with a selected narcotic analgesic. Thus, it would be obvious to substitute T-614 for ibuprofen whether an "unexpected" increase or, alternatively, just a "normal" increase can be obtained.

In addition, as noted above (see [1]) it is submitted that the mere substitution of one component for another to yield predictable results represents a *prima facie* case of obviousness whether a "teaching, suggestion, or motivation" exists or not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *12 (2007).

[3] Applicants argue, "the Baker reference teaches away from substituting iburpfoen with another NSAID ... because of the unexpected synergy that it purports for the combination of ibuprofen with a narcotic analgesic ... [and that substitution] would result in a dosage form which is not directed to the principle of operation described in the Baker reference" (e.g., see

7/17/07 Response, page 7, paragraphs 1 and 2).

[3] "A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Para-Ordnance Mfg. v. SGS Importers Int'l*, 73 F.3d 1085, 1090, 37 USPQ2d 1237, 1241 (Fed. Cir. 1995) (quoting *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994)). The Baker et al. reference does not warn the artisan against using other NSAIDS. To the contrary, the reference states, "[a] continuing goal is to be able to reduce the dosage of such narcotic analgesics by combining them with non-addicting ingredients while still maintaining a high level of analgesia [i.e., whether they exhibit synergistic effects or not]"). That is, the reference doesn't state, as purported, "[a] continuing goal is to be able to reduce dosage of such narcotic analgesics by combining them with non-addicting ingredients while still maintaining a high level of analgesia [only if a synergistic relationship can be established]"). Consequently, the "principle of operation" only requires a "reduced dosage" of the narcotic while still maintaining a "high level of analgesia" (e.g., see column 2, lines 5-10). That is exactly what T-614 delivers (e.g., see rejection above disclosing superior analgesic potency, as compared to ibuprofen). Thus, a person of ordinary skill in the art would expect to be able to "reduce the dosage" of the narcotic while still maintaining a "high level of analgesia" in accordance with the principle of operation set forth in the Baker et al. reference. Furthermore, the reference provides examples where a synergistic relationship between narcotic and the analgesic are not even required (e.g., see columns Baker et al., columns 1 and 2, especially column 1 lines 30-37, "no evidence or suggestions of other than an additive analgesic effect for the combination [was established for

ibuprofen/codeine]"). In addition, T-614 would also decrease potential side effects such as unwanted gastrointestinal ulcerogenic actions or water/sodium excretions.

In addition, the mere substitution of one analgesic for another does not rise to the level of "substantial" reconstruction or redesign. See *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (Claims were directed to an oil seal comprising a bore engaging portion with outwardly biased resilient spring fingers inserted in a resilient sealing member. The primary reference relied upon in a rejection based on a combination of references disclosed an oil seal wherein the bore engaging portion was reinforced by a cylindrical sheet metal casing. Patentee taught the device required rigidity for operation, whereas the claimed invention required resiliency. The court reversed the rejection holding the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate." 270 F.2d at 813, 123 USPQ at 352.). To the contrary, the courts have held that the mere substitution of one equivalent compound for another to treat the same physiological problem (e.g., T-614 for ibuprofen to treat inflammatory pain) does not represent a "teaching away" or a change in "principle of operation" as purported (e.g., see *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) noted above wherein the court held that it is *prima facie* obvious to combine two (or more) compositions each of which is taught by the prior art to be useful for the same purpose; see also *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *12 (2007)).

Furthermore, the reference must deliberately seek to avoid the proposed change in order to constitute a "teaching away." For example, in *In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988)) a system for measuring minute quantities of nitrogen presumably for the detection of drugs and

explosives was examined. The claims were rejected as being obvious over Eads in view *Warnick*. Eads disclosed a method for separating and identifying sulfur compounds. *Warnick* disclosed a process for detecting pollutants in the atmosphere by measuring the level of nitric oxide. The PTO held that it would have been *prima facie* obvious to substitute the nitric oxide detector of *Warnick* for the sulfur dioxide detector of Eads. On appeal, the Federal Circuit reversed noting that Eads deliberately sought to avoid the use of nitrogen because the sulfur detector was adversely affected by substantial quantities of nitrogen. Thus, according to the CAFC, "instead of suggesting that the system be used to detect nitrogen compounds, Eads deliberately seeks to avoid them; it warns against rather than teaches Fine's invention." See *Id.* at 1599. Thus, *Fine* provides an example of a "teaching away" by disclosing that the presence of a claimed element, nitrogen, is undesirable. No such "teaching away" exists in the present case. That is, Baker never states that T-614 won't work or that it will be undesirable to use it. Therefore, Applicants' arguments are moot.

[4] Applicants argue that the phrase, "[t]his patent discloses that the analgesic effect of the combination of a selected NSAID and a selected narcotic analgesic is greater than for either alone" refers only to the Sunshine reference that is directed to "one of the five structural categories indicated [in that reference]", which presumably does not include T-614 (e.g., see 7/17/07 Response, pages 8 and 9).

[4] The obviousness rejection set forth above is based on the combination of the Baker and Furst, not a combination of Baker and Sunshine. The Sunshine reference only offers examples of prior art. Thus, Applicants' arguments are moot. Furthermore, even if, *assuming*

arguendo, the Sunshine reference was being combined in the manner suggested by Applicants (which is not the case, see above) the result would not change. For example, Furst states that T-614 is a more potent and safer drug then nimesulide, indomethacin and ibuprofen (e.g., see Tanaka et al., page 935, Summary), which indicates that T-614 can be used successful as a substitute for a wide range of NSAIDs including ibuprofen as set forth in Sunshine (e.g., see Sunshine, column 17, line 8 wherein ibuprofen is disclosed), etc. Consequently, a person of ordinary skill in the art would understand after reading the Sunshine reference that T-614 could be used as a substitute for ibuprofen as exemplified in Baker. Finally, it should be noted that the Sunshine reference recites "the compositions and methods of the present invention can be selected from the following categories..." (emphasis added). That is, Sunshine is not limited to only the five categories mentioned at the cited passage as was erroneously reported by Applicants.

[5] Applicants argue, "the Sunshine reference is directed to combinations of caffeine and NSAIDs; caffeine and narcotic analgesics; and caffeine and NSAIDs/narcotic analgesics." (e.g., see 7/17/07 Response, page 8, paragraph 3).

[5] Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references. Here, Applicants state that Sunshine contains caffeine but fail to state how this distinguishes the presently claimed invention. Furthermore it is additionally noted that the Sunshine reference is not being relied upon in the present rejection and, as a result, Applicants' arguments are moot

(i.e., the rejection is based on Baker and Tanaka, not Baker and Sunshine).

[6] Applicants argue, "it is improper for the Examiner to rely solely on the Background of the Invention of the Baker reference" noting that the "entire" reference must be considered including portions that "teach away" from the claimed invention (e.g., see 7/17/07 Response, paragraph bridging pages 9 and 10 and first full paragraph on page 10).

[6] The Examiner contends that this "teaching away" argument was adequately addressed in at least section [3] above.

[7] Applicants argue, "Tanaka reference does not definitively conclude that [T-614] is equally efficacious as ibuprofen ... [noting] Section 4.2.1 of the Tanaka reference, which states that '[t]he analgesic potency of T-614 in rats was equal to that of nimesulide and weaker than those of indomethacin and ibuprofen' ... When viewing the Tanaka reference in its entirety, Applicants submit that this reference does not definitively conclude [T-614] is equally efficacious as ibuprofen" (e.g., see 7/17/07 Response, bottom of page 9 to top of page 10).

[7] The Examiner respectfully disagrees. Tanaka et al. summarized "all" of their results on page 935 stating, "The antiinflammatory, analgesic and antipyretic activities of ... T-614 ... were ... compared with those of nimesulide, indomethacin and ibuprofen. The anti-inflammatory potency of T-614 ... was greater than that of ibuprofen." Thus, it is Applicants, not the Examiner, who has failed to appreciate the reference as a "whole" by focusing in one or two studies instead of the collection of studies as "summarized" by the authors. Furthermore, Tanaka et al. go on to conclude, "One of the most interesting results was that T-614 had virtually

no gastrointestinal ulcerogenic action which is known as a common side-effect for NSAIDs ... Moreover, T-614 does not show any acute toxic effects even at a oral dose of 5 g/kg" (e.g., see Tanaka et al., page 944, last paragraph). Thus, a person of ordinary skill in the art would be motivated to use T-614 even if it could be shown to be weaker than ibuprofen because it is a safer drug.

[8] Applicants argue, "The Examiner is relying on an improper 'obvious to try' rationale" (e.g., see 7/17/07 Response, page 11, section d).

[8] The Examiner respectfully disagrees. The Supreme Court has recently put a stop to this kind of "rigid preventive rules" in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *7 (2007) ("the Court of Appeals ... conclude[d], in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try" ... Rigid preventative rules that deny fact finders recourse to common sense, however, are neither necessary under our [Supreme Court] case law nor consistent with it").

[9] Applicants argue, "In re O'Farrel is analogous to the present situation, where one of ordinary skill in the art would have to try each of numerous possible NSAIDs in place of ibuprofen in order to arrive at the selection of [T-614]" (e.g., see 7/17/07 Response, page 11, section d).

[9] An invention is "obvious to try" where the prior art provides either no indication of which parameters would be critical or no direction as to which of many possible choices is likely to be successful. *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807, 10 USPQ2d 1843, 1845

(Fed. Cir.), cert. denied, 493 U.S. 975 (1989) (quoting *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)), which is clearly not the case here. Tanaka, for example, explicitly states that T-614 is a good replacement for ibuprofen (e.g., see Tanaka, Summary; see also concluding paragraph). Thus, the critical factors (i.e., potency and safety) have been well delineated by the prior art and the possible choices have been narrowed to just one (i.e., T-614).

[10] Applicants argue, "The Examiner is improperly picking and choosing [T-614] and oxycodone from the prior art ... it appears that the inventors in the Baker reference rejected all NSAIDs in their invention except ibuprofen" and cited various passages in the Baker reference in support of this position (e.g., see 7/17/07 Response, page 11-16).

[10] There's no evidence to suggest that Baker et al. knew anything about the benefits of T-614. Therefore, it cannot be said that Baker et al. "rejected all NSAIDS in their invention except ibuprofen." Furthermore, to the extent that applicants have impliedly argued that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Here, Tanaka et al. provide ample motivation/expectation for success for making the T-614/ibuprofen substitution (e.g., see Tanaka et al., Summary; wherein Tanaka et al. disclose greater anti-inflammatory potency and fewer side effects for T-614). Thus, Tanaka et al. provide a strong motivating force (e.g., increased potency

with decreased side effects) that would impel one skilled in the art to do what applicant are currently claiming (*Ex parte Levengood*, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Int. 1993)). In addition, a person of ordinary skill in the art would not have to "pick and choose" from among a wide range of variables to construct the currently claimed invention as purported because Tanka et al. only disclose favorable interactions between T-614 and ibuprofen, which is the preferred embodiment disclosed in the Baker et al. reference.

[11] Applicants argue, "The Examiner is improperly relying on In re Kerkhoven ... wherein the court held that it is prima facie obvious to combine two (or more) compositions each of which is taught by the prior art to be useful for the same purpose ... However, the Examiner's rejection, is based on modifying the Baker analgesic composition" (e.g., see 7/17/07 Response, page 17, paragraph 2).

[11] The Examiner contends that even if, assuming arguendo, Kerkhoven stands for the position set forth by Applicants, it would not change the overall result because Tanaka provides ample motivation to make the substitution. Furthermore, even if, assuming arguendo, Tanaka does not provide ample motivation (which is not the case, see above), the Supreme Court has spoken on this issue by stating that simple substitutions with predictable results represents a prima facie case of obviousness whether a "teaching, suggestion, or motivation" is found or not. See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 2007 WL 1237837, at *12 (2007).

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

5. Claim 38, 47-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et

al. '937 and Tanaka et al., as applied to claims 38, 47, 48 and 50-52 above, and further in view of Oshlack et al. US Pat. No. 5,472,712 (12/95) or Oshlack et al. US Pat. No. 6,294,195 (9/01: effectively filed 10/93 or earlier).

The substance of the above obviousness rejection is hereby incorporated by reference in its entirety.

Although the Baker reference teaches oral dosage forms that include "sustained release" formulations (e.g. tablets, capsules, etc: see col. 3-4, especially col. 4) utilizing "sustained release carriers", the Baker reference fails to explicitly teach "a sustained release carrier which provides a sustained release of the oxycodone and/or ... salt thereof".

However, the use of sustained release dosage forms for opioid analgesics, including oxycodone which utilize sustained release carriers employing beads which are coated with the opioid drug or which include substrate layers which include the drugs is known in the art to effectuate delayed release of extended duration. E.g. see Oshlack et al. and Oshlack patent references.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize sustained release carriers for oxycodone including beads/layers as taught by the Oshlack and Oshlack et al. patents for use in the Baker compositions since Baker specifically teaches using "sustained release formulations" and further in view of the advantages of utilizing the Oshlack patent sustained release carriers including delayed drug release of extended duration.

Response

6. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "for the reasons discussed above, the baker reference [and] Tanaka reference fail to teach or suggest the presently claimed method ... [and] Oshlack ... fail to cure the deficiencies [of these references" (e.g., see 7/17/07 Response, pages 17 and 18).

This is not found persuasive for the following reasons:

The Examiner contends that to the extent that Applicants are simply repeating their previous arguments, those issues were adequately addressed in the above sections (which are incorporated in their entireties herein by reference).

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON EPPERSON
PRIMARY EXAMINER